A CLINICAL STUDY OF CHLORIDE EXCRETORY FUNCTION.

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Introduction. The purpose of this investigation has been to study the value, as a clinical test, of the method of measuring sodium chloride excretory function, recently introduced by McLean.[1]

McLean has modified the formula devised by Ambard and Weill[2] to express the laws of excretion of sodium chloride in normal individuals, so that, given the data of rate of excretion of urine, concentration of chloride in the urine and the body weight of the subject, the concentration of chloride which would be found in the blood plasma could be calculated, provided the excretory function was normal. This modified formula is expressed as follows:

$$\text{Plasma chloride} = 5.62 + \sqrt{\frac{\text{Gm. NaCl per day}\ \sqrt{\text{Gm. NaCl per liter}}}{4.23 \times \text{body weight in kilos.}}}$$

The figure 5.62 refers to the normal threshold for chlorides, or concentration in the plasma at which excretion begins. Ambard and Weill found that excretion began when the concentration of chlorides in the blood plasma had risen above 5.62 per liter. The figure 4.23 is a constant introduced into the formula.

The theoretical concentration of plasma chloride calculated from the formula may then be compared with the actual concentration found by analysis of the blood plasma. The supposed threshold of beginning excretion for any case under study may be calculated from the following formula:

$$\text{Threshold} = \text{plasma chloride} - \sqrt{\frac{\text{Gm. NaCl per day}\ \sqrt{\text{Gm. NaCl per liter}}}{4.23 \times \text{body weight in kilos.}}}$$

McLean found in a large series of examinations in normal individuals that the theoretical concentration corresponded fairly closely with the concentration actually found. He then applied the method to the study of pathological conditions[3] and found that relatively increased concentration of chlorides in the plasma occurs especially in certain forms of cardiac and renal disease; that edema is usually accompanied by a relatively increased concentration of chlorides in the plasma, also that chloride and urea functions may be quite independent of one another.

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[1] Jour. Exper. Med., 1915, xxii, 234.

[2] Semaine méd., 1912, xxxii, 217.

[3] McLean, F. C.: Jour. Exper. Med., 1915, xxxii, 366.

The method of studying chloride excretory function hitherto most generally employed has been the test of the ability of the kidneys to excrete salt added to the diet. The patient is put upon a constant daily chloride intake until equilibrium between intake and excretion is established. Then on a certain day, 10 grams additional sodium chloride are given. If less than 85 per cent. of the added chloride is excreted within forty-eight hours it is interpreted as a retention.

Frothingham[4] studied 40 cases of chronic nephritis, comparing the test of ability of the kidney to excrete added salt with certain other diagnostic and prognostic tests of renal disease. Of the 40 cases, but one showed no impairment of ability to excrete added salt, whereas 14 excreted phthalein in normal amount. Frothingham's table shows that 9 of the cases with normal phthalein had very markedly impaired ability to excrete the added chlorides. Frothingham concluded that the added salt test is the best functional test for the detection of early chronic nephritis, but that it is of not much value in prognosis, since the ability to excrete added chloride may be greatly impaired relatively early in the course of the disease.

O'Hare[5] has studied 15 cases of nephritis by McLean's method of testing chloride excretory function and compared the results with those obtained by the Hedinger and Schlayer two-hour renal test and test of ability to excrete added chloride. He concludes that the McLean test is more satisfactory than the others.

Although the added salt test is undoubtedly of great value in the study of nephritis, it has many obvious disadvantages. The patient should be in a hospital, preferably under the care of a nurse trained specially to give metabolic diets. The test requires five or six days' time to be carried out properly. During this time all the urine must be carefully saved. If, as not infrequently occurs in nephritic cases, the patient vomits after the administration of the added salt the test is lost. Thus its application must be limited almost entirely to the comparatively small proportion of cases that can be studied in hospitals. On the other hand the method of studying excretion of chloride devised by McLean is relatively easy to carry out. It is not dependent upon any diet. It requires but two analyses. It does not necessitate having the patient in a hospital subject to the expense and loss of time incident to the added salt test. Therefore, if by the McLean test equally satisfactory information as to renal adequacy for chloride excretion could be obtained, it would be well worth adopting as a clinical test. For this reason we have tried the method in a series of cases, which have received careful clinical study and whose renal function has been tested by other methods.

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[4] Am. Journ. Med. Sc., 1915, cxlix, 808.

[5] Arch. Int. Med., 1916, xvii, 711.

METHODS. The technic of collecting specimens was carried out as recommended by McLean. The procedure was instituted usually three to four hours after the last meal. The patient was given 180 c.c. of water to drink. Thirty minutes later a seventy-two minute collection of urine was begun. In the middle of this period, blood was withdrawn and immediately shaken with a few crystals of potassium oxalate to prevent clotting. If the patient was unable to void exactly at the end of the seventy-two minute period, the period during which the urine was collected was noted to the nearest minute. The urine was measured to the nearest cubic centimeter. The blood was centrifuged for twenty minutes at high speed. The plasma was drawn off by pipette and analyzed for chloride content according to the method of McLean and Van Slyke.[6] The standard solutions were tested frequently to ensure their accuracy. Two c.c. portions of plasma were used. Nearly all the tests were made in duplicate. The urinary chlorides were determined by a modified Volhard method.

During the course of the work my attention was called by Dr. J. Harold Austin to the variability in the carbon dioxide binding capacity of plasma when no precautions have been taken to prevent escape of carbon dioxide from the whole blood. Gürber,[7] Petry[8] and others have noted that if the carbon dioxide tension of the serum were increased the cells became richer in chloride. If carbon dioxide is permitted to escape from the whole blood the plasma becomes more alkaline, so that in the mechanism of reëstablishing equilibrium of acids and bases between plasma and cells the chloride goes over from cells to plasma probably in the form of hydrochloride acid. Consequently when no attempt has been made to prevent the escape of carbon dioxide from the whole blood the chloride content of the plasma is found 0.200 to 0.500 grams per liter higher than when this loss of carbon dioxide has been prevented. The amount of migration of chloride from cells to plasma is directly dependent upon the amount of escape of carbon dioxide from the whole blood. Thus while the method of taking blood, which was recommended by McLean, is permissible for clinical determination in which small variation in threshold is not to be regarded as of great significance, a source of error is excluded by preventing the escape of carbon dioxide from the whole blood. To prevent this escape of carbon dioxide, and consequently the variable amount of migration of chloride from cells to plasma, the method of withdrawing blood under albolene, recommended by Van Slyke[9] for determination of carbon dioxide combining power of the plasma, was used in the latter part of the work. Taking this precaution the normal plasma chloride threshold is found to be approximately 5.30 grams per liter instead of 5.62 grams per liter.

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[6] Jour. Biol. Chem., 1915, xxi, 361.

[7] Sitzungsb. d. phys-med. Gesellsch. zu Würzburg, 1895, 28-37.

[8] Hofmeister's Beitrage, 1902, iii, 260.

[9] Personal communication to Dr. J. H. Austin.

I. *Non-nephritic Group without Chloride Accumulation.* In Table I is presented a group of 10 cases supposedly without nephritis or any circulatory disturbance in the kidneys. In this group the difference between the actual and theoretical concentration of plasma chloride has varied between −0.18 and +0.12 grams per liter. McLean, in a series of seventy-two observations, found slightly greater variations.

TABLE I.—NON-NEPHRITIC GROUP WITHOUT CHLORIDE ACCUMULATION.

Case.	Age.	Sex.	Diagnosis.	Sodium chloride, grams per liter.			
				Actual.	Calculated.	Difference.	Threshold.
I	46	M.	Angina pectoris	5.87	5.88	−0.01	5.61
II	29	M.	Endothelioma of lymph nodes	5.90	5.96	−0.06	5.56
III	25	M.	Traumatic epilepsy	6.17	6.26	−0.09	5.53
IV	23	M.	Luetic aortitis	5.87	5.83	+0.04	5.66
V	63	M.	Tumor of pons	5.63[10]	5.57[10]	+0.06	5.36[10]
VI	30	M.	Gastric neurosis	5.97	6.05	−0.08	5.54
VII	26	M.	Streptococcic bacteremia	5.81	5.96	−0.15	5.47
VIII	57	M.	Chronic myocardial disease; arteriosclerosis	5.81	5.88	−0.07	5.55
IX	16	F.	Bronchial asthma	5.56	5.72	−0.18	5.44
X	57	M.	Arteriosclerosis	5.59[10]	5.47 •	+0.12	5.42 •

II. *Non-nephritic Group with Chloride Accumulation.* In Table II are included 8 cases which show elevated chloride threshold, although they were considered after careful study in the hospital to be non-nephritic.

Cases XI and XII.—Entered the hospital with edema, due to cardiac decompensation. On admission both showed high threshold for chlorides. After the edema had subsided the threshold returned to normal.

Case XIII.—The chloride studies were made in this case of luetic cirrhosis of the liver, during a period when the patient had marked ascites, bilateral hydrothorax, and edema of the legs. At that time the phthalein excretion was 20 per cent. in two hours. The urine contained a cloud of albumin. Later when the collections of fluid has disappeared the phthalein rose to 60 per cent.; the urine showed only a faint trace of albumin. The retention of chlorides was probably due to circulatory disturbances in the kidneys.

Case XIV.—Diagnosis: cardiac decompensation, secondary cirrhosis of the liver. When the chloride study was made the patient's abdomen was steadily filling with fluid. There was almost complete anuria. After withdrawal of most of the fluid a fair urinary excretion was established. Tests made at this time showed the chloride threshold very much lower.

[10] Blood taken under albolene.

Case XV.—This case apparently belongs to the type described by Christian[11] as having disturbed salt elimination, but not, strictly speaking, actual nephritis. This man gave a history of always having eaten large amounts of salt. To test his statement a twenty-four hour specimen of urine examined for sodium chloride content while he was on the ordinary ward diet showed 29 grams. The chloride threshold was markedly above the normal on two examinations. During this time he had slight edema. He was then placed on a fixed low chloride intake and weighed every day at exactly the same time. On the day 10 grams sodium chloride was added to the diet he weighed 1.5 kilos more than on the preceding day. On that day none of the added chloride was excreted. On the following day, however, 7.9 grams extra chloride was excreted. This man has continued under observation for five months on a somewhat limited salt intake. He has shown no further tendency to edema.

Case XVI.—This case was diagnosed as probable early renal tuberculosis. The urine never showed more than a trace of albumin. The phthalein excretion was 35 per cent. in two hours. Two c.c. indigo-carmine were injected intravenously and the ureteral orifices observed for evidence of excretion. At the end of eight minutes a faint blue stream was seen coming from the left ureter. The amount was not materially increased at the end of twenty minutes. No excretion was observed from the right ureter in twenty minutes. Therefore, whatever may have been the primary disease the case had actual renal inadequacy when these studies were made. The elevated threshold for chlorides may be considered as one of the expressions of this inadequacy.

Case XVII.—The elevated chloride threshold in this case is difficult to explain. The urine examination, blood-pressure readings, phthalein tests, and blood urea analysis gave no evidences of nephritis. The patient was voiding only from 400 c.c. to 660 c.c. urine for several days before the first test of chloride excretory function was made. He was then given theocin, 0.2 gram three times a day for three days and the studies repeated. The plasma chloride, meanwhile, had dropped 0.5 milligram per cubic centimeter. However, the chloride threshold was still elevated above the normal.

Case XVIII.—This case also gave no evidences of renal inadequacy. The diagnosis made was chronic myocardial disease with anginoid attacks. The statement was made by the patient's physician that there had been edema of the legs before admission to the hospital. None, however, was observed during his stay in the ward. No material change in the threshold was observed after giving theocin, 0.2 gram, three times a day for three days or after tincture of digitalis, 0.65 c.c., three times a day for five days. The only suggestive finding in this case was the fact, that the urinary concentration of chloride was always low.

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[11] Christian, H. A.: Am. Jour. Med. Sc., 1916, cli, 630.

TABLE II.—CASES PRESUMABLY NON-NEPHRITIC WITH CHLORIDE ACCUMULATION.

Case.	Age.	Sex.	Date.	Diagnosis.	Edema.	Sodium chloride, grams per liter of plasma.			
						Actual.	Calculated.	Difference.	Threshold.
XI	63	M.	Oct. 26	Cardiac decompensation	+	6.25	5.86	+0.39	6.01
			Nov. 16		0	6.00	5.92	+0.08	5.70
XII	36	M.	Nov. 2	Cardiac decompensation	+	6.69	5.88	+0.81	6.43
			4		+	6.69	5.95	+0.74	6.36
			16		0	6.43	6.29	+0.14	5.76
XIII	42	M.	Nov. 21	Luetic cirrhosis	+	6.34	5.84	+0.50	6.12
XIV	67	F.	Jan. 7	Cardiac decompensation; secondary cirrhosis	+	6.65	5.68	+0.97	6.59
			Mar. 24		+	6.31	5.88	+0.43	6.05
XV	26	M.	Dec. 20	Bronchial asthma	+	6.62	6.19	+0.43	6.05
			23			6.50	5.99	+0.51	6.13
XVI	28	F.	Feb. 22	Renal tuberculosis (?)	0	6.12[12]	5.63[12]	+0.49	5.79[12]
XVII	50	M.	Nov. 8	Sciatica	0	6.81	5.95	+0.86	6.48
			18			6.31[13]	5.84	+0.47	6.09
XVIII	63	M.	Nov. 8	Myocardial weakness	+	6.37	5.84	+0.53	6.15
			18			6.31[13]	5.77	+0.54	6.16

III. *Chloride Excretory Function in Nephritis.* In Table III are presented the results of study in 22 cases of nephritis, arranged according to the clinical classification employed in the University Hospital.

Advanced Glomerulonephritis: Of 11 cases studied, 9 showed high chloride threshold. Of this group 3 cases (XX, XXIV, and XXVI) showed no lowering of chloride threshold under the influence of vapor baths and salt-free diet.

CASE XIX, whose threshold was high when the first studies were made after nineteen days' treatment with salt-free diet and vapor baths, showed a drop of 0.78 gram chloride per liter of plasma. Two days after the administration of 10 grams of sodium chloride, a slight amount of which was vomited, the threshold had again risen slightly beyond its original point. Case XXVIII, in addition to advanced nephritis, on admission had slight cardiac decompensation with edema of the legs. Under rest and digitalis the edema rapidly disappeared, but a hematuria which had been quite marked on admission, persisted. The patient was then put upon salt and protein-low diet and given a hot pack every other day. The hematuria gradually diminished until there were no macroscopic evidences of blood in the urine. Erythrocytes could still be found under the microscope, however. A McLean test at this time showed that the threshold was not raised above the normal limit. As a check upon this finding the test of ability to excrete 10 grains additional sodium chloride was made. But 4.9 grams were excreted in forty-eight hours. The urine which had been clear for about two weeks previously, on the day chloride was administered, became quite hemorrhagic in appearance. The red color gradually disappeared in the course of a week.

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[12] Blood withdrawn under albolene.

[13] Had received theocin for three days.

CASES XIX and XXVIII. These cases illustrate the point that the finding of a normal chloride threshold must not be regarded as conclusive evidence that the kidney function for chloride excretion is normal. In Case XXVIII the sudden return of hematuria after the administration of sodium chloride suggests very strongly that the salt acted as a renal irritant.

CASE XXIX.—This patient, who had the greatest waste nitrogen retention of any case in the group, showed no accumulation of chloride in the plasma. A test of ability to excrete added chloride could not be carried out as the patient was bordering on uremia. In this case the diagnosis of advanced glomerulonephritis was confirmed by autopsy a few weeks after the patient had left the hospital.

Thus of 11 cases of diagnosed clinically as advanced glomerulonephritis, 9 showed impairment of renal chloride excretory function by having a high chloride threshold, a tenth showed no elevation of the threshold, but impairment of ability to excrete added sodium chloride, while the eleventh, one of the most severe cases in the group, showed a normal plasma chloride, but could not be studied as to his ability to excrete added chloride.

Intermediate Glomerulonephritis. In this group of 4 cases 2 showed a high threshold for chlorides.

CASE XXXI.—This case is of interest because the plasma chloride threshold was high, whereas the ability to excrete added salt was practically unimpaired. On admission to the hospital this patient had advanced neuroretinitis with many hemorrhages. The blood-pressure was 200 systolic and 110 diastolic. The urine showed a faint trace of albumin with only an occasional cast. The specific gravity tended between 1.005 and 1.009, but on a dry diet rose to to 1.028. The blood nitrogen was 28 milligram per 100 c.c. The phthalein excretion was 55 per cent. in two hours. The plasma chloride threshold at this time was 6.44 grams per liter. Of 10 grams added salt, 7.9 grams were excreted in forty-eight hours. The patient was kept quietly in bed on a salt-free low protein diet. The retinitis improved slowly. The blood-pressure fell to 145 systolic and 88 diastolic. Headache, which had been a troublesome feature of the case, disappeared. The improvement has continued over a period of six months, during which time the patient has been on a restricted salt intake.

Early Glomerulonephritis. One case, diagnosed early glomerulonephritis, was studied, as follows:

CASE XXXIV.—This patient came to the hospital, to the service of Dr. de Schweinitz, complaining of dimness of vision. He was found to have a peculiar form of proliferative retinitis, apparently not of renal origin. Physical examination was entirely negative, except for slight enlargement of the heart to the left, accentuated aortic second sound, and slight sclerosis of the peripheral arteries. The blood-pressure was only slightly elevated.

TABLE III.—GROUP OF NEPHRITIC CASES.

Case.	Age.	Sex.	Date.	Sodium chloride, grams per liter.				Urine.			Blood-pressure.		Phthalein per cent.	Non-protein blood, mgr. in 100 c.c.	Blood urea, mgr. in 100 c.c.	Eye-ground examination.
				Actual.	Calculated.	Difference.	Threshold.	Albumin.	Casts.	Specific gravity.	Systolic.	Diastolic.				
ADVANCED GLOMERULONEPHRITIS.																
XIX	39	F.	Apr. 17	6.03[11]	5.50[11]	+0.53	5.83[11]	Cloud	Few	1.008-1.011	200	140	1		102	Renal retinitis.
			27	5.69[11]												
			Mar. 6	5.25[11]	...	...	...	....	..	....	250	160				
			Mar. 26	6.03[11]	5.32[11]	−0.71	6.01[11]									
XX	44	M.	Feb. 25	6.25[11]	5.42[11]	+0.83	6.13[11]	Cloud	Many	1.010-1.012	210	135	Trace	......	142	Angiosclerosis.
			Mar. 4	6.22[11]	5.47[11]	+0.75	6.05[11]	....	..	....	178	120	7			
			8	6.22[11]	5.53[11]	+0.60	5.09[11]									
XXI	40	F.	Dec. 4	6.81	5.90	+0.91	6.53	Cloud	Many	1.009-1.010	204	138	Trace	......	220	
XXII	47	F.	Dec. 18	6.47	5.75	+0.72	6.34	Cloud	Many	1.012-1.015	202	141	15	......	83	Neuroretinitis.
XXIII	30	M.	Oct. 20	6.62	5.70	+0.92	6.54	Cloud	Many	1.009-1.013	186	115	Trace	76	....	Angiosclerosis.
			Nov. 1	6.19	5.64	+0.55	6.17	....	..	....	135	97				
XXIV	63	M.	Nov. 30	6.00	5.73	+0.27	5.89	Trace	Many	1.010-1.012	225	105	12	......	90	Neuroretinitis.
			Dec. 4	6.02	5.65	+0.37	5.99									
			17	6.22	5.81	+0.41	6.03	....	..	....	....	....	15	......	115	
XXV	35	M.	Nov. 20	6.47	5.87	+0.60	6.22	Trace	Occas.	1.010-1.027	190	102	25	56	....	Disk, margins blurred; one hemorrhage.
			Dec. 3	6.37	5.81	+0.56	6.18									
XXVI	24	M.	Nov. 4	6.12	5.71	+0.41	6.03	Heavy	Many	1.010-1.025	242	180	33	40	....	Wide-spread retinitis.
			15	6.12	5.82	+0.30	5.02	....	..	....	178	135	37			
			29	6.25	5.81	+0.44	6.06	Cloud								
			Dec. 3	6.28	5.74	+0.54	6.16									
XXVII	45	M.	Feb. 8	6.09	5.69	+0.40	6.02	Light cloud	Few	1.015-1.010	185	135	35	......	39	Hemorrhages; neuroretinitis
XXVIII	34	M.	Mar. 21	5.53[11]	5.43	+0.12	5.42	Light cloud	Very few	1.005-1.014	182	78	12	......	80	Negative.
											138	40	20			
XXIX	34	M.	Mar. 27	5.48[11]	...	...	...	Cloud	Many	1.009-1.011	175	110	Trace	......	417	Negative.
			29	5.50[11]												
INTERMEDIATE GLOMERULONEPHRITIS.																
XXX	24	M.	Feb. 1	6.41	5.99	+0.42	6.04	Cloud	Many	1.013-1.015	160	120	30	...	90	
XXXI	48	F.	Dec. 21	6.56	5.74	+0.82	6.44	Trace	Few	1.005-1.020	200-145	110-88	55-68	28	....	Neuroretinitis.
XXXII	24	F.	Feb. 10	5.62[11]	5.54[11]	+0.08	5.38[11]	Faint trace	None	1.010-1.012	190	135	35	......	31	Angiosclerosis.
XXXIII	30	M.	Mar. 9	5.66[11]	5.55[11]	+0.11	5.41[11]	Cloud	Many	1.012-1.025	170	110	55	......	37	Angiosclerosis
EARLY GLOMERULONEPHRITIS.																
XXXIV	39	M.	May 27	5.75[11]	5.46[11]	+0.29	5.59[11]	None	None	1.021	155	102	56	......	25	Proliferative retinitis.
CHRONIC DEGENERATIVE NEPHRITIS.																
XXXVI	29	F.	Apr. 17	6.25[11]	5.62[11]	+0.63	5.93[11]	Boils solid	Many	1.023	150	110	35	......	36	Negative.
			10	6.12[11]	...	...	...	....	..	....	135	90				
			May 4	6.03[11]												
XXXVII	34	M.	Jan. 22	6.37	5.96	+0.41	6.03	Cloud	Many	1.028	....	....	60	......	60	Old hemorrhages.
XXXVIII	58	M.	June 4	6.40[11]	5.33[11]	+1.07	6.37[11]	0 gm. per liter	Many	1.015	160	90	Trace	......	261	Slight angiosclerosis.
RENAL SCLEROSIS.																
XXXIX	55	M.	Nov. 27	6.12	6.02	+0.10	5.72	Faint trace	Few	1.031	....	....	52	......	48	Negative.
XL	63	F.	Mar. 11	5.78[11]	5.66[11]	+0.12	5.42[11]	Cloud	Many	1.009-1.035	250	130	35	......	....	Angiosclerosis.
ACUTE PYELONEPHRITIS.																
XLI	37	F.	Nov. 8	5.62	5.51	−0.11	5.51	Cloud	None	1.010-1.015	110	65	10 Trace	187	442	

[11] Blood taken under albolene.

Numerous urine examinations failed to show either albumin or casts. The phthalein excretion was normal. There was no accumulation of urea in the blood. The sodium chloride threshold was only slightly elevated. The ability to excrete added sodium chloride was markedly diminished, but 2 out of 10 grams added salt being excreted in forty-eight hours. The degree of impairment of renal function for chlorides revealed by the inability to excrete added chlorides would scarcely have been suspected from the very slight elevation of the threshold.

Chronic Degenerative Nephritis. But 3 cases diagnosed as chronic degenerative nephritis were studied. All showed a high threshold. The chloride excretion seemed more disturbed than the phthalein or urea excretion, except in Case XXXVIII, in whom almost all kidney function had ceased.

Renal Sclerosis. The 2 cases diagnosed renal sclerosis studied, showed no retention of chloride.

Acute Pyelonephritis.

Case XLI.—This was a case of acute pyelonephritis; the urine contained a large amount of pus and gave pure culture of Bacillus mucosus capsulatus. It is of interest chiefly because of the low chloride threshold in contrast to a tremendous retention of urea and a phthalein excretion varying from 10 per cent. to a trace. The diagnosis of acute pyelonephritis was confirmed by autopsy.

Poisoning by Mercuric Chloride.

TABLE IV.—POISONING BY MERCURIC CHLORIDE.[14]

Case.	Days after taking mercuric chl.	Sodium chloride, grams per liter.				Urine.		Phthalein percentage.	Remarks.
		Actual.	Calculated.	Difference.	Threshold.	Albumin.	Casts.		
XLIII	1	4.56	5.30	−0.74	4.56	Cloud	Many	10	Modified Lambert treatment. 8th day Lambert treat. dis.
	2	4.62	5.30	−0.68	4.62	"	"	25	
	4	4.92	5.30	−0.38	4.92	"	"	65	
	9	5.50	5.31	+0.19	5.49	Light cloud	None	43	
	14	5.81	5.40	+0.41	5.71	Faint trace	Occasional	48	
XLIV	1	5.25	5.44	−0.19	5.11	Trace	"	7	Lambert treatment dis. 5th day.
	4	5.27	5.36	−0.09	5.21	"	None	50	
	9	5.87	5.46	+0.41	5.71	"	"	55	

Case XLIII (Table IV).—White, male, age twenty-one years, weight 60 kilos. Took 0.5 gram mercuric chloride, thinking it was a headache remedy. Fifteen minutes later he discovered his mistake, took seven eggs, some starch, and milk. Brought immediately to the hospital, where a modified Lambert treatment was instituted within an hour of the time he had taken the mercuric chloride. During the first twenty-four hours he voided over 4000 c.c. of urine. For several days the urine showed enormous numbers of casts and renal epithelium and a cloud of albumin. The phthalein, which had been low, returned to normal until the Lambert treatment was discontinued, when it dropped slightly again. The blood urea never rose above 0.43 gram per liter.

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[14] All blood taken under albolene.

The concentration of chlorides in the plasma after twenty-four hours of the Lambert treatment dropped to 4.56 grams per liter the lowest figure that has been found in the laboratory. The urine at the time showed only a faint trace of chlorides, not sufficient to determine quantitatively by the McLean and Van Slyke method for chlorides. Three days later there was a slight rise in concentration of chlorides in the plasma, but still only a trace of chloride in the urine. After the Lambert treatment was discontinued and a diet containing more salt given the plasma chloride rose rapidly until there was evidence of distinct retention.

Case XLIV (Table IV).—White, male, aged twenty-four years, weight 69 kilos. While intoxicated he took 0.5 gram mercuric chloride dissolved in 150 c.c. of water. Vomited about three hours later. Then came to the hospital, where a modified Lambert treatment was instituted immediately. There was good diuresis, 3200 c.c. of urine passed in the first twenty-four-hour period. The phthalein was 7 per cent. at the first examination, but subsequently rose to normal. The urine never showed more than a trace of albumin and a few hyaline and granular casts. Highest blood urea figure 0.300 gram per liter.

The behavior of the chloride in the case resembled that of Case I. During the Lambert treatment the concentration in plasma was below the normal threshold. After the Lambert treatment was stopped there was distinct retention of the chlorides.

These cases of mercurial poisoning show how a concentration of chloride in the plasma below a normal threshold may be reached by vigorous measures of elimination. In both cases at the time the urine examinations and phthalein excretion showed most damage to the kidney the plasma chloride concentration was well below the normal threshold. Later, when the evidences of nephritis had subsided, the Lambert treatment discontinued and the patient allowed to take a diet containing salt, the concentration of chloride in the plasma quickly rose to a point where it was quite evident that there was distinct retention.

Eclampsia. Through the kindness of Dr. B. C. Hirst it was possible to study the plasma chloride in 5 cases of eclampsia and 2 cases bordering on eclampsia. Unfortunately in 2 of the cases the condition of the patient was such that accurate studies of urinary excretion could not be carried out.

The 5 cases of eclampsia all show a high plasma chloride concentration. Three in whom urinary studies could be carried out showed marked elevation of chloride threshold. In Case XLV (Table V), studied while rapid improvement was taking place, the plasma chloride fell 0.22 milligram per cubic centimeter in twenty-four hours. The two preëclamptics also showed chloride retention;

in 1 case, quite marked; in the other, which was probably a combination of preëxisting nephritis and threatened eclampsia, not so marked. This chloride retention is in contrast to the very slight tendency for waste nitrogen to be retained in eclampsia.

TABLE V.—ECLAMPSIA.

Case.	Date.	Blood-pressure.		Blood urea. Mgm. per 100 c.c.	Sodium chloride, grams per liter of plasma.			
		Systolic.	Diastolic.		Actual.	Calculated.	Difference.	Threshold.
XLV	Mar. 29	205	135	30	6.00[16] 5.78[16]			
XLVI	Feb. 28				6.37	5.71	+0.66	6.28
XLVII	Feb. 26	138	105		5.76[16]	5.30[16]	+0.40	5.70[16]
XLVIII	Feb. 3			46	6.53			
XLIX	Dec. 30	220	196	26	6.62	5.94	+0.68	6.30
			THREATENED ECLAMPSIA.					
L	May 14	180	130	44	6.00[16]	5.32[16]	+0.68	5.98[16]
LI	May 14	220	145	64	5.69[16]	5.33[16]	+0.36	5.66[16]

DISCUSSION. While the McLean method of studying renal chloride excretory function seems to give valuable information in many cases of nephritis, the results in each particular case must be regarded critically. Two cases of advanced nephritis in this series had marked impairment of their ability to excrete salt, yet the threshold at various times was found normal. On the other hand 2 cases with a very high threshold were able to sweep out added salt very efficiently. While a normal threshold does not necessarily signify that renal function for chlorides is unimpaired, a high threshold probably nearly always means impaired chloride excretion, whether this be due to actual renal disease or circulatory deficiency.

The marked effect produced by conditions interfering with the circulation in the kidney, such as passive congestion, must always be borne in mind. The threshold may be quite as high in cases of cardiac decompensation with edema as in the severest cases of advanced nephritis. The excretion of chloride is apparently far more influenced by passive congestion than is the excretion of urea.

The results of the work here presented agree in a general way with the conclusion of McLean that the chloride and urea functions may be quite independent of one another. Retention of chloride without retention of urea occurs very much more frequently than the reverse. But 2 cases were found in the series, in which there was a high blood urea figure and normal chloride threshold. Since both these cases were very ill, so that no other tests of renal adequacy for chlorides could be carried out, it is doubtful whether these cases really had good renal function for chlorides.

SUMMARY. A study of the method of investigating renal excretory function devised by McLean has been made in a series of normal and pathological cases.

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[16] Blood taken under albolene.

The application of Van Slyke's method of withdrawing blood to prevent escape of carbon dioxide and the effect of this procedure upon the chloride content of the plasma were discussed.

A group of individuals with presumably normal renal function was found to conform fairly closely, in the excretion of chlorides, to the laws of excretion formulated by Ambard and Weill.

A group of cases diagnosed as non-nephritic showed elevated threshold for chlorides. Most of these cases showed evidences of circulatory disturbances in the kidneys.

Studies of chloride excretory function were made in 21 cases of nephritis, 7 cases of eclampsia and threatened eclampsia, and 2 cases of mercuric chloride poisoning.

CONCLUSIONS. · 1. An elevated plasma chloride threshold, when circulatory disturbances can be excluded, is valuable evidence of the presence of nephritis.

2. A normal threshold may be found in cases with marked impairment of ability to excrete chlorides, particularly if the patient has been kept on a regime including salt-free diet and measures to stimulate elimination.

3. Sodium chloride added to the diet is sometimes excreted as completely by impaired kidneys working under the stimulation of a high chloride content of the plasma as by normal kidneys working under normal threshold; added chloride may be retained when the threshold is normal. Therefore the information gained by both methods of study is desirable,.

4. Chloride excretory function is impaired in nearly all cases of nephritis.

5. Chloride excretory function is much more disturbed in eclampsia then is urea excretory function.

FAMILIAL EPISTAXIS; A CASE REPORT.[1]

By Henry B. Richardson, M.D.,

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Osler, in 1901[2] described a "family form of recurring epistaxis, associated with multiple telangiectases of the skin and mucous membranes." Since then he has collected from the literature and from his own experience, data on eight families afflicted with the disease.[3] Hutchinson and Oliver[4] recently reported a remarkable family, in which it occurred in three successive generations. Osler's description well sums up the disease. Its hereditary nature is particularly striking. Neither sex predominates. The attacks of

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[1] From the Medical Clinic of the Peter Bent Brigham Hospital.

[2] Johns Hopkins Hosp. Bull., 1901, xii, 333.

[3] Ibid., 1907, xviii, 402.

[4] Quart. Jour. of Med., 1916, ix, 67.